The physiology of wound healing

It is vital that practitioners are able to relate their knowledge of wound physiology to everyday clinical practice. This review therefore summarises the main features of the physiological processes of wound healing

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Physiology; Wound healing

Wound healing is a complex physiological process that is dependent on a number of inter-related factors. Wound assessment and treatment should be based on an understanding of normal tissue repair and factors affecting the process.

The process of wound healing

All tissues in the body are capable of healing by one of two mechanisms: regeneration or repair. Regeneration is the replacement of damaged tissues by identical cells and is more limited than repair. In humans, complete regeneration occurs in a limited number of cells — for example, epithelial, liver and nerve cells. The main healing mechanism is repair where damaged tissue is replaced by connective tissue which then forms a scar. Wound healing can be defined as the physiology by which the body replaces and restores function to damaged tissues.[1]

Local conditions for good wound healing

The provision of a supportive microenvironment at the wound surface is of the utmost importance when trying to maximise a wound's healing potential.[2] Maintaining a controlled set of local conditions that is able to sustain the complex cellular activity occurring in wound healing should be the primary aim of wound management.

In simple terms the process of wound healing can be divided into four dynamic phases: vascular response, inflammatory response, proliferation and maturation. There is considerable overlap between these phases, and the time needed by an individual to progress to the next phase of healing depends on various factors.[3,4]

Careful assessment should help to identify each stage of wound healing. This is important as treatment objectives may differ as each phase of healing progresses. Inappropriate wound management often occurs due to the practitioner's inability to differentiate between normal and abnormal characteristics associated with wound healing.[5]

The vascular response

Any trauma to the skin which penetrates the dermis will result in bleeding. The damaged ends of blood vessels immediately constrict to minimise blood loss. The exposure of blood to the air helps to initiate the clotting process which is accelerated due to platelet aggregation.

A blood clot is produced by a complex chain reaction called the coagulation cascade. This is characterised by the formation of a fibrin mesh which temporarily closes the wound and gradually dries out to become a scab. At this stage, wounds usually produce large amounts of blood and serous fluid, which help to cleanse the wound of surface contaminants.[1]

The inflammatory response

Tissue damage and the activation of clotting factors during the vascular phase stimulates the release of inflammatory mediators such as prostaglandins and histamine from cells such as mast cells. These mediators cause blood vessels adjacent to the injured area to become more permeable and to vasodilate. This inflammatory response can be detected by the presence of localised heat, swelling, erythema, discomfort and functional disturbance.[1]

Although the clinical signs are similar, inflammation should not be confused with wound infection. The classic signs of inflammation are due to increased blood flow to the area and the accumulation of fluid in the soft tissues.

Wound exudate is produced during this stage of healing due to the increased permeability of the capillary membranes. Exudate contains proteins and a variety of nutrients, growth factors and enzymes which facilitate healing. It also has antimicrobial properties.[6]

Exudate production, which is most prolific during the inflammatory phase of healing, bathes the wound with nutrients and actively cleanses the wound surface. It also acts as a growth medium for phagocytic cells.[7] However, excessive exudate production can cause skin sensitivities and tissue maceration.

Neutrophils are the first type of white blood cell to be attracted into the wound, usually arriving within a few hours of injury. These phagocytic cells have a short life span but provide initial protection against micro-organisms as they engulf and digest foreign bodies.[8]

After 2–3 days macrophages become the predominant leucocyte in the wound bed. Their function at this stage is to cleanse the wound. Macrophages are present throughout all stages of the healing process, producing a variety of substances that regulate healing including growth factors, prostaglandins and complement factors (complex proteins).[9]

Patients who are immunosuppressed are often unable to produce a typical inflammatory response, so may fail to activate the normal healing process.[10]

Slough formation is common during the inflammatory stage and occurs when a collection of dead cellular debris accumulates on the wound surface. It may be creamy yellow due to the large amounts of leucocytes present. Chronic wounds may develop areas of fibrous tissue cover ing the wound base. This often combines with slough, making it harder to remove.

Formation of new tissue in the wound bed will not occur until the macrophages have stimulated the proliferative phase by the release of growth factors and the wound bed has been sufficiently cleansed by the inflammatory process.[11] Macrophages are responsible for control-

ling the transition between the inflammatory and proliferative phases of healing.[12]

The proliferative stage

During this phase the wound is filled with new connective tissue. A decrease in wound size is achieved by a combination of the physiological processes of granulation, contraction and epithelialisation.

The formation of granulation tissue

Granulation is the term used to describe the new wound matrix made up of collagen and an extracellular material called ground substance. These provide the scaffolding into which new capillaries will grow to form connective tissue.

The growth of new blood vessels is termed angiogenesis. This is stimulated by macrophage activity and tissue hypoxia resulting from the disruption of blood flow at the time of injury. The role of oxygen in wound healing is complex and not yet fully understood. It may be significantly different in epidermal and connective tissue repair.[13]

Macrophages produce a variety of substances that stimulate angiogenesis. These include transforming growth factor (TGF), which promotes formation of new tissue and blood vessels, and tumour necrosing factor (TNF), which facilitates the breakdown of necrotic tissue, stimulating proliferation.[9]

Healthy granulation tissue does not bleed easily and is a pinky red colour. The condition of granulation tissue is often a good indicator as to how the wound is healing. Granulation tissue which is dark in colour may signal that the wound is ischaemic or infected.[14]

Wound contraction

After connective tissue production, fibroblasts congregate around the wound margin. They contract, pulling the wound's edges together. This plays a significant part in the healing of large, open wounds.[15]

Re-epithelialisation

The re-growth of epithelial cells across the wound surface occurs during the final stage of proliferation. A moist wound environment accelerates this process, enabling epithelial cells to migrate more easily.[16] The progress of epithelial migration is significantly slowed in the presence of necrotic tissue or a scab as epithelial cells are forced to burrow underneath the eschar which forms a mechanical obstruction in the wound bed. The mitotic activity of cells within a wound is sensitive to local fluctuations in temperature and is significantly slowed down at temperature extremes.[17,18]

In wounds healing by secondary intention epithelialisation occurs once granulation tissue fills the wound bed. New epithelial cells, which have a translucent appearance and are usually whitish-pink, originate from the wound margin or from the remnants of hair follicles, sebaceous or sweat glands. They divide and migrate along the surface of the granulation tissue until they form a continuous layer.[19]

The maturation stage

In healthy individuals this stage begins approximately 20 days after injury and can last for many months, or even years in complex wounds.[8] Initially scar tissue is raised and reddish. As the scar matures, its blood supply decreases and it becomes flatter, paler and smoother.

Mature scar tissue is avascular and contains no hairs, sebaceous or sweat glands. Scar formation is a normal consequence of the process of tissue repair in adults. Foetal wounds have been shown to heal without the production of scar tissue.[20]

Remodelling of scar tissue is stimulated by macrophages and results in the reorganisation of collagen fibres to maximise tensile strength.[12] The tensile strength of scar tissue compared with normal skin is about 80%.[15]

The formation of keloid and hypertrophic (raised) scars are abnormalities associated with this stage of healing. Hypertrophic scarring occurs directly after initial repair, while keloid scarring may occur some time after healing.[21] Keloid scars continue to grow and spread, invading surrounding healthy tissue, whereas hypertrophic scars do not. Black Afro-Caribbean people are 10 times more likely to develop keloid scarring than Caucasians.[21]

Delayed wound healing

Many factors can significantly delay healing. Often the exact mechanism of delay is not well understood and requires further investigation.[4] The general health of an individual will influence their ability to heal normally and chronic diseases affect wound healing in different ways. Conditions resulting in reduced tissue perfusion, metabolic disturbances or malabsorption syndromes contribute to delayed repair.[22] Local factors such as wound infection, mechanical stress, use of toxic cleansing agents and the presence of foreign bodies can also prolong healing.[3] Finally, socio-economic and psychological factors can also slow the rate of repair.[23]

Conclusion

To maximise wound healing potential, practitioners need to relate their knowledge of wound physiology to everyday clinical practice. When assessing wounds, nurses must take account of the balance between the physical and psychosocial influences that can affect healing. ■

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